The indication that the rejections over the prior art have been withdrawn and that claim 26 is allowed is noted with appreciation. The sole rejection remaining is the rejection of claims 20, 22-25, 27-30 and 36-45 under 35 USC 112, first paragraph, for alleged lack of enablement. Applicants respectfully traverse this rejection.

In support of the rejection, the Examiner contends that (a) the specification as filed does not provide evidence regarding the effect of OPV vaccination on high-risk individuals, and (b) Hviid et al provide evidence that one category of high-risk children (those with at least one sibling with IDDM) show increased risk of IDDM with OPV vaccination. With respect to contention (a), Applicants submit herewith the Declaration under 37 CFR 1.132 of Professor Heikki Hyoty, which includes test results showing that OPV is effective in reducing the risk of type 1 diabetes (IDDM) in high risk individuals. With respect to contention (b), Applicants respectfully submit that the Hviid et al article does not provide sufficient reason to cast doubt on the accuracy of Applicants' presumptively accurate disclosure, as next discussed.

Hviid et al make reference to speculation that childhood vaccinations could influence the development of type 1 diabetes because, with the introduction of childhood vaccinations in developed countries, the incidence of type 1 diabetes has increased. Hviid et al also present opposite opinions (Hviid et al at page 1399, left column, second paragraph: "However, the majority of the evidence does not provide support for these specific hypotheses or for any other association between type 1 diabetes and childhood vaccination, yet there have been few analytic studies.")

Hviid et al evaluated whether there is any relation between type 1 diabetes and routinely administered childhood vaccinations. They studied a cohort comprising all children born in Denmark between 1990 and 2000, and a subgroup of children having a sibling with type 1 diabetes (Hviid et al at page 1399, left column, second and third paragraphs). They found no casual relationship between childhood vaccination and type 1 diabetes (see the conclusion in the abstract, at the bottom of page 1398). From Table 2 at page 1402 it might seem that increased doses of OPV increased the risk of diabetes in the risk group, but it should be noted that the number of cases was so small, that it lacks statistical significance, which is also noted by the authors (Hviid et al at page 1403, left column, second full paragraph; "Although we found that the risk of type 1 diabetes increased among children who had one or more siblings with diabetes, there was no apparent association between diabetes and vaccination among such children. However, the lack of statistical significance and inconsistency limit the conclusions that can be drawn from this analysis.")

In addition, there is a methodological issue in the article by Hvidd, which makes it difficult to interpret the results. Applicants submit herewith a copy of EPI News No. 15, 2002, which shows the vaccination coverage of polio vaccination (IPV and OPV) in Denmark. The coverage of IPV was almost 100% and of OPV over 90%. In view of this and taking into account that Denmark has a population of about 5 million people, and a nativity of about 1.2%, it is unclear what the unvaccinated group is in the Hvidd article, and whether on the whole it is big enough for statistical comparison. It even appears that the authors might have compared unvaccinated ages with vaccinated ages of the same children, which is problematic when the

outbreak of type 1 diabetes may take several years from the vaccination.

With specific respect to claims 23 and 24, Applicants respectfully note that Hviid et al studied the effect of routine vaccination, which in Denmark comprises polio vaccination with **IPV** at an early age, followed by OPV at 2, 3 or 4 years of age. This is completely different from the claimed invention, where early immunization with OPV, preferably starting by the age of three months, is recommended (cf. Claim 24, and the immunization regime set forth at page 11 of the specification). According to the invention defined by all claims the vaccination regime is based on OPV and not IPV, and, with respect to claims 23 and 24, the OPV is given in early infancy. The effect of this regime against non-polio enteroviruses and type 1 diabetes is based on the replication of live OPV viruses in the recipient. As a live vaccine, OPV induces strong T-cell response, which mediates the protection against non-polio enteroviruses and type 1 diabetes. IPV vaccine lacks this property and induces mainly antibodies.

In view of the above, it is respectfully submitted that (a) the Hviid et al article does not provide sufficient reason to cast doubt on the accuracy of Applicants' presumptively accurate disclosure and (b) the evidence of record in the Declaration submitted herewith would, in any event, be sufficient to overcome any alleged *prima facie* case of lack of enablement set forth by the Hviid et al article. Accordingly, it is respectfully submitted that the sole remaining rejection of record has been successfully traversed and should be withdrawn.

Accordingly, it is respectfully submitted that all rejections and objections of record have been overcome and that the application is now in allowable form. An early notice of allowance is earnestly solicited and is believed to be fully warranted.

Respectfully submitted,

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